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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Nobuko Uchida

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EXAMINER

SINGH, ANOOP KUMAR

ART UNIT

PAPER NUMBER

1632

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/568,568	<b>Applicant(s)</b> UCHIDA ET AL.	
	<b>Examiner</b> ANOOP SINGH	<b>Art Unit</b> 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 16 October 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-52 is/are pending in the application.
- 4a) Of the above claim(s) 1-48, 50-52 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 49 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/5/07; 10/29/07</u> .                                       | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

This action is in response to the papers filed October 16, 2008. Applicant's response to restriction requirement to the claims filed October 16, 2008 has been entered. Applicants' amendments to the specification and abstract filed 2/15/2006 have been received and entered.

Currently, claims 1-52 are pending.

### ***Election/Restrictions***

Applicant's election without traverse of claim 49 (group VIII) in the reply filed on October 27, 2008 is acknowledged. It is noted that claims 50-51 and 52 have not been rejoined with the elected group as they are directed to distinct population of progenitor cells that are committed to the endocrine beta cell lineage. Applicants also elected monoclonal antibody AC133 with traverse. Applicants' argument that it would not be undue burden to search other species of monoclonal antibody was found persuasive; therefore, election of species requirement between species of antibody is hereby withdrawn. As the restriction is still deemed proper, the requirement for restriction is maintained and hereby made FINAL.

Claims 1-48, 50-52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic claim. Election was made **without** traverse in the reply filed on October 29, 2008.

Claim 49 is under examination.

### ***Specification***

The disclosure is objected to because of the following informalities: The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code (for example see pages 16, line 16, page 15, lines 21-22). See MPEP § 608.01. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 49 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. In the instant case, claim 49 is directed to a pancreatic stem cell that expresses inherent characteristic markers present on a native pancreatic stem cell in the pancreatic tissue of any mammal. The fact that the claimed pancreatic stem cells can be separated from the pancreas of a mammal does not necessarily mean that it is separated. Therefore, claim 49 encompasses a naturally occurring pancreatic stem cell that would inherently express characteristics markers. In the absence of the hand of man, the naturally occurring products are deemed natural and non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). See MPEP 2105. As such, the recitation of the limitation "an isolated pancreatic stem cell" would be remedial.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be

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patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Abraham et al (Diabetes, June 2003, Vol. 52 (1), A357, IDS) and Yu et al (The Journal of Biological Chemistry, 2002, 20711-20716, IDS).

Claim is directed to a pancreatic stem cell, wherein the pancreatic stem cell is CD133+CD49f+ cell.

With respect to claim 49, Abraham et al teach islet-derived pancreatic stem cell that is capable of differentiating into pancreatic endocrine and exocrine phenotype that are positive for CD29 and CD49f meeting the limitation of the claim (see abstract). It is noted that the pancreatic stem cell disclosed by Abraham et al is derived from pancreatic tissue and express marker CD49f that is structurally and functionally similar to one disclosed in the instant application. Additionally, it is also disclosed that the pancreatic stem cell population disclosed by Abraham et al contains very small percentage of the cell that may be positive for CD133.

Therefore, pancreatic stem cell population disclosed by Abraham et al must contain

cells that are positive for both CD49f and other markers including CD133 in same native pancreatic stem cell. As stated in MPEP 2112: The express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. "The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness." *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir.1995) (affirmed a 35 U.S.C. 103 rejection based in part on inherent disclosure in one of the references). See also *In re Grasselli*, 713 F.2d 731, 739, 218 USPQ 769, 775 (Fed. Cir. 1983).

While Abraham et al. describe a CD49f+ pancreatic stem cell, but differed from claimed invention by not disclosing cell being positive for CD133.

However, use of different markers to further characterize non hematopoietic stem cell was routine in art. For instance, Yu et al teach AC133 (CD133) is expressed in pancreatic tissue that could be used to characterize non hematopoietic cells or tissue (see abstract, page 20713, col. 2, para. 2). Yu et al reported that CD133 (AC133) is expressed in stem cell niche (see page 20716, col. 1, para.) and is found to be co expressed with CD29 (beta 1 integrin). Additionally, Yu et al also teach FACS to sort CD133 positive cell (see page 20712, col. 2, para. 3).

Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine the respective teachings of Abraham et al., Yu et al. to further characterize pancreatic stem cell positive for CD29Cd49f by looking the expression of CD133, with a reasonable expectation of success, at the time of the instant invention. A person of skill in the art would have been motivated to characterize implicit characteristics of pancreatic stem cells, as a matter of design choice to further characterize pancreatic stem cell in order to obtain enriched population of pancreatic stem cell for transplantation as disclosed by Abraham, said design choice amounting to combining prior art elements according to known methods to yield predictable results. One who would practiced the invention would have had reasonable expectation of success because Abraham had already disclosed

a Cd49f positive pancreatic stem cell in a NIP population that also contained small number of CD133 positive cell, while Yu reported CD133 expression in non hematopoietic tissue such as pancreas that could be used to further characterize cells and was found to be co expressed with CD29. Thus, it would have only required routine experimentation for one of ordinary skill in the art to further characterize the pancreatic stem cells disclosed by Abraham by sorting the pancreatic stem cells using the known methods with other markers including CD 133 to obtain a CD49fCD133 positive pancreatic stem cell. It is noted that [T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property, or other markers CD133 which is implicitly present in the prior art pancreatic stem cell, does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ430, 433 (CCPA 1977).

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zulewaski et al (Diabetes 50:521-533, 2001, IDS) or Taniguchi et al (WO/2002/088335, dated 11/7/2002, abstract), Nakauchi et al (US Patent no. 7,150,990, dated 12/19/2006, filed on 3/6/2002 and Yu et al (The Journal of Biological Chemistry, 2002, 20711-20716, IDS).

Claim is directed to a pancreatic stem cell, wherein the pancreatic stem cell is Cd133+CD49f+ cell. It is noted that Examiner has relied on a U.S. published application no. 20050003529 as being an English translation of the cited Japanese

WIPO document WO/2002/088335, while relying solely on the WIPO document for the rejection.

With respect to claim 49, Zulewaski et al teach a nestin positive islet-derived progenitor stem cell population that is capable of differentiating into pancreatic endocrine, exocrine and hepatic phenotype and are positive for CK 9, neural adhesion molecule (see abstract and page 522, col. 1, par. 1, figure 2). Similarly, Taniguchi et al teach a pancreatic stem cell derived from the pancreas of a mammal and also disclose analyzing the state of expression of multiple markers to characterize the cell (see abstract). It is noted that the pancreatic stem cells disclosed by Zulewaski et al/ Taniguchi et al are derived from pancreatic tissue that are structurally and functionally similar to one disclosed in the instant application. Therefore, pancreatic stem cell disclosed by Zulewaski et al/ Taniguchi et al must implicitly express markers such as Cd49f and CD133 present on native pancreatic stem cell. As stated in MPEP 2112: The express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. "The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness." *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir.1995) (affirmed a 35 U.S.C. 103 rejection based in part on inherent disclosure in one of the references). See also *In re Grasselli*, 713 F.2d 731, 739, 218 USPQ 769, 775 (Fed. Cir. 1983). Although, Zulewaski et al/ Taniguchi et al describe pancreatic stem cells derived from pancreas, but differed from claimed invention by not disclosing stem cell positive for CD49f CD133.

Prior to instant invention, Yu et al teach AC133 (CD133) is expressed in pancreatic tissue that could be used to characterize non hematopoietic tissue (see abstract, page 20713, col. 2, para. 2). Yu et al reported that CD133 (AC133) is expressed in stem cell niche (see page 20716, col. 1, para.) and is found to be co expressed with CD29 (beta 1 integrin). Yu et al also teach FACS method to sort CD133 positive cell (see page 20712, col. 2, para. 3), while Nakauchi et al reported



CD49f as one of the marker for pluripotent stem cells capable of differentiating into pancreatic ductal cell (see claim 1-3 of Nakauchi).

Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine the respective teachings of Zulewaski /Taniguchi, Yu et al. and Nakauchi et al to further characterize pancreatic stem cell by looking the expression of CD133 and CD49f, with a reasonable expectation of success, at the time of the instant invention. A person of skill in the art would have been motivated to further characterize implicit characteristics of pancreatic stem cells, as a matter of design choice to further characterize pancreatic stem cell in order to obtain enriched population of stem cell for transplantation therapy as disclosed by Zulewaski, said design choice amounting to combining prior art elements according to known methods to yield predictable results. One who would practiced the invention would have had reasonable expectation of success because Zulewaski/Taniguchi had already disclosed a pancreatic stem cell, while Yu and Nakauchi reported expression of CD133 and CD49f in the pancreatic cells. Thus, it would have only required routine experimentation for one of ordinary skill in the art to further characterize the pancreatic stem cells disclosed by Zulewaski/ Taniguchi by further characterizing the pancreatic stem cells using the known methods with other markers including CD 133 and Cd49f to obtain CD49fCD133 positive pancreatic stem cells.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

### ***Conclusion***

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANOOP SINGH whose telephone number is (571)272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272- 4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anoop Singh/  
Examiner, Art Unit 1632